Remarks

Applicants appreciate the withdrawal of the rejection under 35 U.S.C. § 112.

The claims are further amended in this submission to specify that the third, fourth, and fifth divergent regions are, like the second divergent region, at least 10 contiguous nucleotides in length and differ by at least 3 nucleotides from the second divergent region found in *Bradyrhizobium japonicum* 16S rRNA gene. This amendment is supported in the specification at paragraph [23] which teaches: "The divergent regions comprise at least 10 contiguous nucleotides and differ by at least 3, 4, 5, or 6, nucleotides from a divergent region found in *Bradyrhizobium japonicum* 16S rRNA gene." It is respectfully submitted that this amendment adds no new matter and is merely clarifying.

The rejections of claims under § 103(a)

1. Claims 1-3, 7-11, 13-18, 22-26, and 28-42 stand rejected over Greisens and Reischl
2. Claims 4, 12, 19, and 27 stand rejected over Greisen, Reischl, Abrams, Iversen, and Buck
3. Claims 5 and 20 stand rejected over Greisen, Reischl, Kunsch, and Buck
4. Claims 6 and 21 stand rejected over Greisen, Reischl, Barry, and Buck

The Office Action states that the subject claims "are merely drawn to a real-time PCR reaction as taught by Reischl using the primer and probe conditions taught by the primary reference of Greisen et al." The Office Action believes that applicant's patentability rationale relies on improved sensitivity and less contamination, which, the Office Action points out, are

not recited in the claim. However, the distinction between the combination of prior art and the claimed invention lies in the use of a probe to a divergent region to specifically, accurately, and uniquely hybridize to bacterial DNA in a real-time PCR reaction. There was no way to know or predict that this sensitive discrimination would be possible using the real-time PCR reaction.

Greisen teaches the use of probes to hybridize to a 16S rRNA gene region in a Southern blot, but not in a real-time PCR reaction. Reischl teaches the use of probes to hybridize to other gene regions which are non-divergent among bacteria. Reischl does not teach the ability of a real-time PCR probe to discriminate among multiple similar gene regions, *i.e.,* the divergent regions of the 16S RNA. Even combining Reischl and Greisen's teachings, there was no way to predict that the real-time PCR reaction would permit the sensitive discrimination among various bacteria using a probe to a divergent region of 16S rRNA.

As shown in Example 4 of the subject application, three closely related Staphylococcal species were accurately discriminated using a probe to the divergent region of rRNA. This demonstrates that the discrimination was possible in the real time-PCR assay. Moreover, the presence of other bacteria in a sample did not interfere with the detection. See Table 5. This is a critical feature, affording the advantage of not needing to culture and purify bacteria prior to testing.

None of the cited references suggested a real-time PCR reaction such as the one claimed with one set of primers, a universal probe, and one or more species-specific ("divergent") probes for binding to the amplicon. None of the prior art teaches or suggests that such a reaction would successfully discriminate among bacteria.

Applicants request that all rejections be withdrawn and that the application be speedily allowed.

Respectfully submitted,

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